REMARKS

Claims 1-19, 41, and 43-59 were pending in the instant application. Of these, claims 4-8 and 54 had been previously withdrawn by the Examiner. This Amendment follows a personal interview held September 10, 2003 between Applicants' undersigned attorney, Patrick T. Skacel, and Examiner Ford and her supervisor, Examiner Nita Minnifield. The courtesies extended Applicants' attorney during the interview are sincerely appreciated. The remarks presented herein make of record the issues discussed during the interview.

By this Amendment, Applicants have amended claims 41, 55, and 57 to address the Examiner's concerns, as set forth in the April 22, 2003 Office Action and discussed during the personal interview. These claims now recite that the nucleotide sequence encoding the transporter domain is located downstream from the nucleotide encoding the passenger peptide or polypeptide. Applicants have amended claim 44 to correct its dependency. Support for the claim amendments can be found in the specification and claims as originally filed, specifically, at page 19, *inter alia*, of the specification. The present Amendment introduces no new matter, and thus, its entry is respectfully requested. Upon entry of the present Amendment, claims 1-3, 9-19, 41, 43-53, and 55-59 will be pending and under examination.

April 22, 2003 Final Office Action:

Withdrawal of previous objections and rejections:

The Examiner withdrew the following previous objections and rejections:

a) objection to the Drawings;

b) rejection of claims 1-2, 9-10 and 15-19 under 35 U.S.C. 102(b); and

c) rejection of claims 1-3, 9-10, 41, and 43-59 under 35 U.S.C. 103(a).

In response, Applicants acknowledge and appreciate the withdrawal of the above objection and rejections.

Examiner's Rejection under 35 U.S.C. §102:

The Examiner maintained the rejection of claims 1-2, 9-10, and 15-19 under 35 U.S.C. 102(b), as allegedly being anticipated by Georgiou, et al. Specifically, the Examiner stated that Georgiou teaches a method for producing stable, surface-expressed polypeptides from recombinant gram-negative bacterial cell hosts. The Examiner further stated that the reference teaches chimeric genes which include a targeting DNA sequence encoding a polypeptide capable of targeting and anchoring the fusion polypeptide to a host cell outer membrane (column 3, lines 53-57), a traversing sequence capable of transporting a heterologous or homologous polypeptide through the outer membrane (column 4, lines 4-14) and a DNA segment that encodes any one of a variety of desired polypeptides (column 4, lines 31-33). The Examiner stated that Georgiou, et al. teaches that the chimeric gene when provided with a functional promoter is expressible in gram-negative host (column 4, lines 34-37) and that the recombinant vectors will express fusion polypeptides and will include a functional promoter sequence and a targeting DNA sequence encoding a protein capable of targeting to the outer surface of a gram-negative bacterial host cell (column 4, lines 38-46). The Examiner asserted that the reference teaches fusion of the DNA sequences via a polylinker region (column 5, lines 1-2), and that the transporter sequence may be derived from a membrane spanning

domain of suitable length from any native outer membrane protein of gram-negative bacteria, including outer membrane proteins such as OmpT, FepT, and the like (column 5, lines 49-51). The Examiner concluded that the protease recognition site would be intrinsic or naturally present in the host cell.

The Examiner disagreed with Applicants' prior assertions that Georgiou, et al. does not disclose a polynucleotide comprising a nucleotide sequence that encodes a transporter domain located downstream from a nucleotide sequence that encodes a passenger peptide. The Examiner first indicated that Georgiou, et al. teaches that the targeting sequence is typically positioned downstream of the promoter sequence, that the transmembrane sequence will encode a protein domain capable of transversing the cell outer membrane, and that the vector will also include a DNA sequence which encodes a desired protein. The Examiner then stated that Georgiou, et al. teaches that "this sequence," i.e. the sequence encoding a desired protein, "when positioned downstream of the transmembrane sequence will be expressed on the external surface of the outer membrane, and typically is exposed to the external medium while remaining stably anchored to the membrane surface (column 4, lines 38-57)." Based on this statement, the Examiner then offered the conclusion that Georgiou, et al. therefore teaches "a DNA segment that encodes a transmembrane protein that is downstream from the *targeting* sequence." (Emphasis added).

In response, Applicants respectfully traverse the Examiner's rejection. In reaching the above conclusion, the Examiner appears to have confused the "targeting" sequence with the "passenger" (or "desired protein") sequence. Applicants' claim 1 recites that the transporter domain is located downstream from the passenger domain. As demonstrated by Applicants'attorney during the personal interview, the Georgiou reference in fact teaches the opposite configuration. Georgiou

teaches C-terminal fusions, not N-terminal fusions as embodied in Applicants' claims. More specifically, the Georgiou patent clearly states at column 4, lines 31-37 that the DNA segment that encodes the desired polypeptide (analogous to Applicant's passenger polypeptide) is positioned downstream from the DNA segment encoding the transmembrane sequence (analogous to Applicant's transporter domain). This is the opposite orientation of that recited in Applicants' claim 1.

The Examiner also cited column 4, lines 38-57 of the Georgiou patent in support of her rejection. These lines, however, are consistent with those cited above, and further support Applicants' position with respect to the orientation of domains. Because the Examiner has confused these domains, her conclusion that "Georgiou et al teach a DNA segment that encodes a transmembrane protein that is downstream from the targeting sequence" does not support, and is simply not relevant to, her rejection of claim 1. The "targeting sequence" of Georgiou is analogous to Applicant's "signal peptide sequence", not Applicant's passenger domain. Therefore, not only does Georgiou fail to teach a polynucleotide encoding a transmembrane protein downstream from the passenger domain, as recited in Applicants' claims, but Georgiou in fact teaches the opposite configuration. Therefore, Applicants maintain that claims 1-2, 9-10, and 15-19 are not anticipated by Georgiou. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Examiner's Rejections under 35 U.S.C. §103

The Examiner maintained the rejection of claims 1-3, 9-10, 15-16, 41, 43-53, and 55-59 under 35 U.S.C. §103(a), as being obvious over Georgiou, et al. in view of Benz, et al. and the rejection of claims 1-3, 9-19, 41, 43-53, and 55-59, under 35 U.S.C. §103(a), as being obvious over

Georgiou, et al., in view of Benz, et al. and further in view of Kozono, et al. The Examiner has acknowledged that Georgiou, et al. does not teach the AIDA protein. The Examiner has taken the position, however, that Benz cures this deficiency of Georgiou, et al., and that "[t]here is nothing on the record to show that the combination of teachings would not suggest the claimed invention." Similarly, the Examiner stated that Georgiou and Benz as combined do not teach a passenger polypeptide that is an antibody or antigen-binding domain of antibody, but that Kozono cures this deficiency and that the combination of the teachings suggests the claimed invention.

In response, Applicants respectfully traverse the above rejections under 35 U.S.C. §103. Applicants first point out to the Examiner that by this Amendment, the recitation already present in claim 1 that the transporter domain is located downstream from the passenger domain has been introduced into independent claims 41, 53, and 57. Furthermore, Applicants assert that, contrary to the Examiner's contention, no combination of references cited by the Examiner suggests the claimed invention. The Examiner has relied on Georgiou, et al. as the primary reference in both obviousness rejections. As indicated above in response to the anticipation rejection, Georgiou, et al. refers to a polynucleotide in which the domains analogous to Applicants' transporter and passenger domains are present in a configuration directly opposite that of the Applicants' invention. The references cited by the Examiner provide no motivation to modify the Georgiou reference so drastically by reversing these domains. One of only ordinary skill would not have been motivated to turn a C-terminal fusion as taught by Georgiou into an N-terminal fusion, as claimed by Applicants, especially given Georgiou's purported advantages of its configuration as set forth at column 4, lines 46-57. Even if such a modification were contemplated, there would have been no reasonable expectation that such a configuration could be successfully used in a process for presenting passenger peptides

or polypeptides on the surface of Gram-negative host bacteria. Accordingly, Applicants' claimed invention is not rendered obvious by any combination of references cited by the Examiner. Applicants therefore respectfully request that the Examiner reconsider and withdraw the rejections under 35 U.S.C. §103.

September 10, 2003 Interview

In the September 10, 2003 interview, the Examiners and the Applicants' undersigned attorney discussed the Georgiou reference and its application to the rejected claims, particularly claim 1. The Georgiou reference forms the basis for all of the Examiner's pending rejections. Applicants' attorney demonstrated to the Examiners that the Georgiou reference describes a polynucleotide encoding a transmembrane sequence that is upstream of the desired polypeptide sequence, whereas the Applicants' invention is directed to a configuration in which the transporter domain (analogous to the transmembrane domain) is downstream of the passenger domain (analogous to the desired polypeptide). In short, it was pointed out that the Georgiou reference teaches a sequence having the opposite configuration of that recited in the Applicants' claims, as is particularly clear from the portions of the reference cited by the Examiner, namely column 4, lines 30-57.

The Examiner agreed to reconsider the art rejections, taking into consideration Applicants' comments. Applicants agreed to amend claims 41, 53, and 57 and have done so by this Amendment.

In view of the above amendments and remarks, it is believed that the claims satisfy the requirements of the patent statutes and fully address the Examiner's concerns as set forth in the April 22, 2003 Final Office Action and discussed during the September 10, 2003 personal interview. Reconsideration of the instant application and early notice of allowance therefore are requested. The

Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,

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